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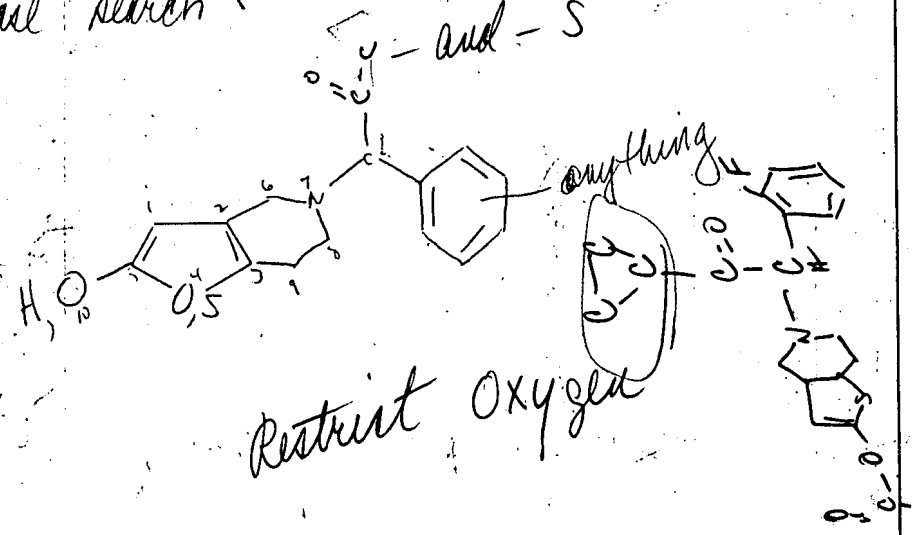

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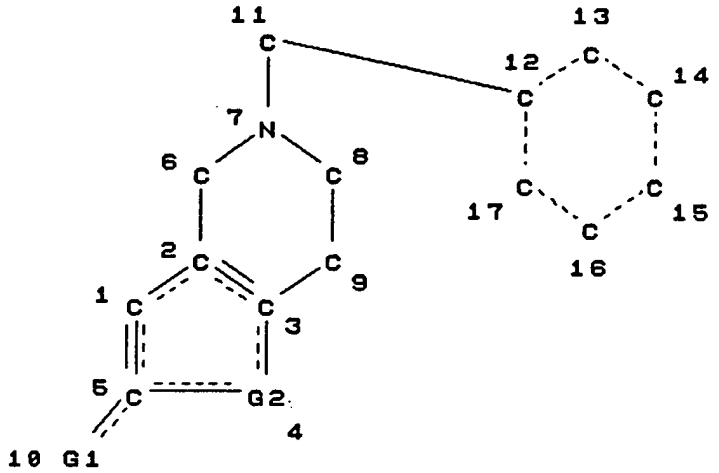

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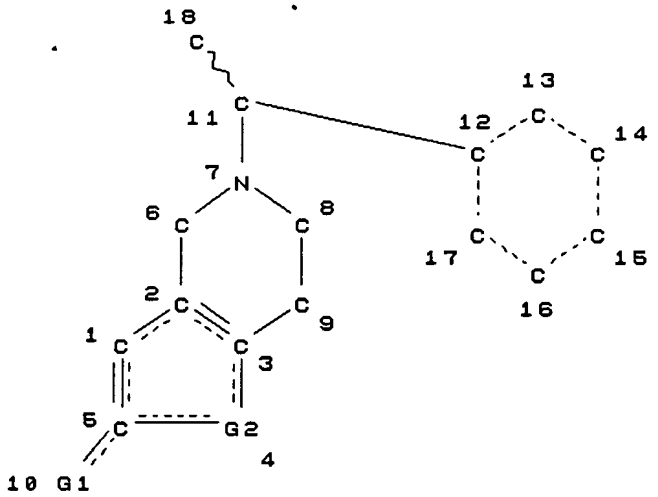

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For OFFLINE Prints or Displays, use the ABS or ALL formats to obtain abstract graphic structures. The AB format DOES NOT display structure diagrams.

L7 21 L6

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L7 ANSWER 1 OF 21 COPYRIGHT 1992 ACS
TI ADP receptor induced activation of guanine nucleotide binding proteins in rat platelet membranes-an effect selectively blocked by the thienopyridine clopidogrel
SO Thromb. Haemostasis, 68(1), 79-83
AU Gachet, C.; Savi, P.; Ohlmann, P.; Maffrand, J. P.; Jakobs, K. H.; Cazenave, J. P.
PY 1992
AN CA117(13):124270s
AB The thienopyridine clopidogrel, a potent analog of ticlopidine, is a powerful inhibitor of ADP induced platelet aggregation and ADP induced inhibition of cAMP accumulation in intact platelets but not of ADP induced shape change. The authors have recently demonstrated that ADP stimulates the binding of GTP.gamma.S to GTP binding

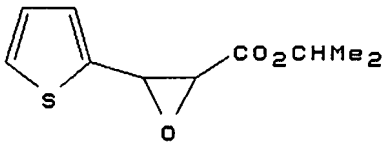
proteins (G proteins) in human platelet membranes. The authors now studied the effects of clopidogrel, a specific inhibitor of ADP induced platelet aggregation on the stimulation of GTP.gamma.S binding to rat platelet membranes by ADP. Using the non hydrolyzable stable analog of ADP, 2MeSADP, the authors demonstrate that 2MeSADP stimulates the binding of [35S]GTP.gamma.S to rat platelet membranes in a concn. dependent manner, that this effect is inhibited by the specific ADP receptor antagonist Sp-ATP.alpha.S and that clopidogrel completely and selectively blocks the stimulation by 2MeSADP of [35S]GTP.gamma.S binding to platelet membranes of treated rats. The authors conclude that: i) rat platelet membranes possess an ADP receptor coupled to unidentified G protein(s) and ii) the thienopyridine clopidogrel impairs the interaction of the ADP receptor with its G protein by an irreversible modification of the ADP receptor itself or its putative G protein.

L7 ANSWER 2 OF 21 COPYRIGHT 1992 ACS
TI Preparation of methyl .alpha.-[4,5,6,7-tetrahydrothieno[3,2-c]pyrid-5-yl]-2'-chlorophenylacetate
SO Eur. Pat. Appl., 9 pp.
AU Descamps, Marcel; Radisson, Joel
PI EP 466569 A1 15 Jan 1992
AI EP 91-401891 8 Jul 1991
PY 1992
AN CA117(9):90266c
AB The title compd. (I) was prepd. Thus, 2-ClC6H4CH(NH2)CO2Me (prepn. from acid given) was condensed with RCH2CH2OSO2C6H4Me-4 (R = 2-thienyl) and the product treated with (+)-camphor-10-sulfonic acid to give, after decompn. of the pptd. salt, (+)-2-ClC6H4CH(CO2Me)NHCH2CH2R (R as above) which was cyclocondensed with HCHO to give (+)-I.HCl (clopidogrel) a known antithrombotic agent.

L7 ANSWER 3 OF 21 COPYRIGHT 1992 ACS
TI Clopidogrel inhibits the binding of ADP analogues to the receptor mediating inhibition of platelet adenylate cyclase
SO Arterioscler. Thromb., 12(4), 430-6
AU Mills, D. C. B.; Puri, R.; Hu, C. J.; Minniti, C.; Grana, G.; Freedman, M. D.; Colman, R. F.; Colman, R. W.
PY 1992
AN CA117(1):565x
AB Clopidogrel, like the homologous thienopyridine deriv. ticlopidine, selectively inhibits platelet aggregation induced by ADP. The authors have previously described two nucleotide-binding sites on platelets related to ADP-mediated platelet responses. The first is a high-affinity binding site for 2-methylthio-ADP (2-MeSADP) that is linked to the inhibition of stimulated adenylate cyclase. The second is the 100-kd exofacial membrane protein aggregin, which is labeled by the reactive ADP analog 5'-p-fluorosulfonylbenzoyl adenosine (FSBA) that is related to shape change and aggregation. The authors set out to det. if either of these sites is blocked in vivo by clopidogrel or its active metabolite. Six subjects were given clopidogrel (75 mg/day for 10 days) in a double-blind crossover expt. All of the subjects developed prolonged bleeding times while taking the drug. The rate of onset of the effect on bleeding time varied among subjects. Platelet aggregation induced by ADP or thrombin was significantly impaired by the drug treatment, but no effect was detected on shape change. The incorporation of [3H]FSBA into aggregin was also unaffected. Inhibition of adenylate cyclase by ADP or by 2-MeSADP was greatly reduced in all subjects, and in the case of 2-MeSADP, there was evidence for a noncompetitive effect. Inhibition of adenylate cyclase by epinephrine was unaffected. In the three subjects for whom binding measurements were

made, the no. of binding sites for [32P]2-MeSADP was reduced from 534 mols. per platelet during control and placebo periods (11 detns.) to 199 mols. per platelet during drug treatment (three detns.). There was no consistent change in the binding affinity. The inhibition of platelet function by clopidogrel is assocd. with a selective redn. in the no. of functional receptors mediating the inhibition of stimulated adenylate cyclase activity by ADP.

L7 ANSWER 4 OF 21 COPYRIGHT 1992 ACS
TI Isopropyl 2-thienylglycidate, process for its preparation, and its use as synthetic intermediate for ticlopidine and clopidogrel
SO Eur. Pat. Appl., 11 pp.
AU Bousquet, Andre; Calet, Serge; Heymes, Alain
PI EP 465358 A1 8 Jan 1992
AI EP 91-401833 3 Jul 1991
PY 1992
AN CA116(19):194139j
GI



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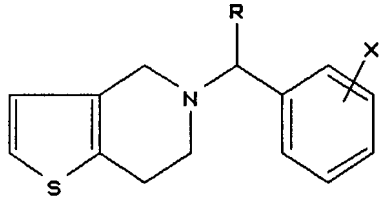
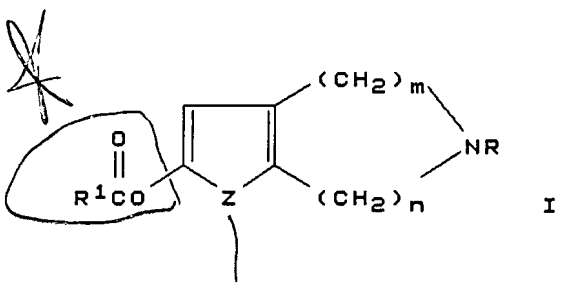


II

AB Title ester I, useful as an intermediate for antithrombotic/platelet antiaggregant thienopyridine derivs. II (R = H, CO2R1; R1 = C1-4 alkyl; X = H, halo), was prepd. Thus, reaction of thiophene-2-carboxaldehyde with ClCH2CO2CHMe2 in Me2CHOH contg. Me2CHONa at 20.degree., with workup and vacuum distn., gave 93% I. Sapon. of I and reaction with NH2OH.HCl (may also be performed in situ with prepn.) gave 95% 2-thienylacetaldoxime, which underwent hydrogenation to the amine (91.5%), conversion to the formimine (100%), and cyclization (93%) to give 4,5,6,7-tetrahydrothieno[3,2-c]pyridine-HCl. This underwent neutralization (100%) and benzylation with 2-ClC6H4CH2Cl (83%) to give ticlopidine-HCl, i.e. II-HCl (R = H, X = 2-Cl). Prepn. of clopidogrel-H2SO4 is also described.

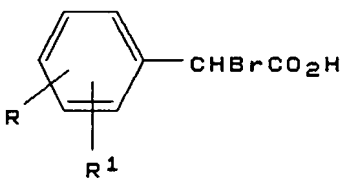
L7 ANSWER 5 OF 21 COPYRIGHT 1992 ACS
TI Preparation of tetrahydrothienopyridines and analogs as elastase and platelet aggregation inhibitors
SO Eur. Pat. Appl., 22 pp.
AU Badorc, Alain; Bordes, Marie Francoise; Frehel, Daniel; Herbert, Jean Marc
PI EP 421861 A1 10 Apr 1991
AI EP 90-402711 1 Oct 1990
PY 1991
AN CA115(17):183262x
GI



I

AB The title compds. I [R3 = alkyl, Ph, benzyl; R = H, CHR2R5; R1 = R3, OR3; R2 = H, alkyl, CO2R4, etc.; R4 = H, alkyl, benzyl; R5 = H, alkyl, (substituted) Ph; Z = S, O; m, n = 1, 2], elastase inhibitors and platelet aggregation inhibitors useful in the treatment of inflammation, were prepd. Treatment of 5-(2-chlorobenzyl)-5,6,7,7a-tetrahydro-4H-thieno[3,2-c]pyridin-2-one with BuLi, followed by reaction with pivaloyl chloride, gave I (Z = S; m = 1; n = 2; R = CHR2R5; R2 = H; R5 = 2-ClC6H4; R1 = Me3C), which at 100 mg/kg gave 61% inhibition of ADP-induced platelet aggregation (animal species unspecified).

L7 ANSWER 6 OF 21 COPYRIGHT 1992 ACS
TI Process for preparing phenylacetic derivatives of thienopyridines and intermediate .alpha.-bromophenylacetic acids
SO Eur. Pat. Appl., 7 pp.
AU Bouisset, Michel; Radisson, Joel
PI EP 420706 A2 3 Apr 1991
AI EP 90-401828 26 Jun 1990
PY 1991
AN CA115(11):114486m
GI



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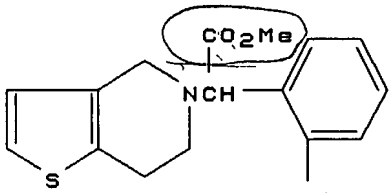
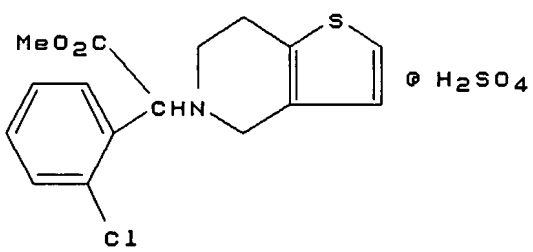


II

AB Brommophenylacetic acids I (R, R1 = H, halogen) were prepd. from RR1C6H3CHO and CHBr3 in the presence of KOH. Thus, 2-ClC6H4CHO was treated with CHBr3 and KOH in dioxane-ice to give 63% 2-ClC6H4CHBrCO2H which was converted to its Me ester and treated with 4,5,6,7-tetrahydrothieno[3,2-c]pyridine to give the thienopyridylacetate II.

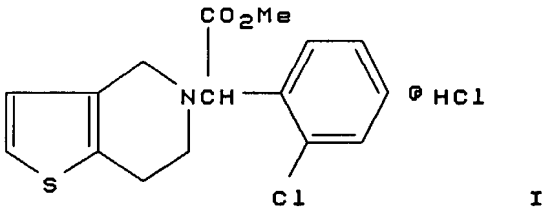
L7 ANSWER 7 OF 21 COPYRIGHT 1992 ACS
TI Ticlopidine and clopidogrel (SR 25990C) selectively neutralize ADP inhibition of PGE1-activated platelet adenylate cyclase in rats and rabbits
SO Thromb. Haemostasis, 65(2), 186-90
AU Defreyn, G.; Gachet, C.; Savi, P.; Driot, F.; Cazenave, J. P.; Maffrand, J. P.
PY 1991
AN CA115(7):64295a
GI



I

AB Ticlopidine and its potent analog, clopidogrel (I), are are powerful inhibitors of ADP-induced platelet aggregation. To understanding of this ADP-selectivity, the authors the these compds. ticlopidine and clopidogrel isomers (SR 25989C and SR 25990C SR 25989C on PGE1-stimulated adenylate cyclase and on the inhibition of this enzyme by ADP, thrombin were studied. and thrombin. Neither drug changed the basal cAMP levels nor the kinetics of cAMP accumulation upon PGE1-stimulation in rat or rabbit platelets, which excludes any direct effect on adenylate cyclase or on cyclic nucleotide phosphodiesterase. However, the drop in cAMP levels obsd. after addn. of ADP to PGE1-stimulated control platelets was inhibited in platelets from treated animals. In contrast, the drop in cAMP levels produced by epinephrine was not previously by either drug in rabbit platelets. In rat platelets, thrombin inhibited the PGE1-induced cAMP elevation but this effect seems to be entirely mediated by the released ADP. Under these conditions, clopidogrel also potently inhibited the effect of thrombin on platelet adenylate cyclase. In conclusion, ticlopidine and clopidogrel selectively neutralize the ADP inhibition of PGE1-activated platelet adenylate cyclase in rats and rabbits.

L7 ANSWER 8 OF 21 COPYRIGHT 1992 ACS
TI The thienopyridine PCR 4099 selectively inhibits ADP-induced platelet aggregation and fibrinogen binding without modifying the membrane glycoprotein IIb-IIIa complex in rat and in man
SO Biochem. Pharmacol., 40(2), 229-38
AU Gachet, Christian; Stierle, Anita; Cazenave, Jean Pierre; Ohlmann, Philippe; Lanza, Francois; Bouloux, Cyrille; Maffrand, Jean Pierre
PY 1990
AN CA113(19):165151q
GI



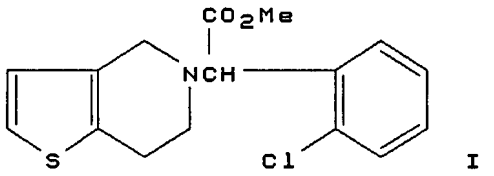
I

AB The effects on platelet functions of PCR 4099 (I) in rat and in man were studied. The aim of the study was to check the possibility of a direct modification of the fibrinogen binding site on the glycoprotein (GP) IIb-IIIa complex. Washed platelet suspensions were used for aggregation and fibrinogen binding studies. Platelet lysates were submitted to SDS-polyacrylamide gel electrophoresis, crossed immunoelectrophoresis and immunopptn. Administration of PCR 4099 inhibited selectively and irreversibly ADP-induced aggregation. Although the effect of ADP on aggregation was blocked, PCR 4099 did not modify ADP-induced shape change. Only the effects of low concns. of thrombin on platelet aggregation were inhibited. Fibrinogen binding was dramatically inhibited in rat and in man when platelets were stimulated with ADP and low concns. of thrombin. At a high concn. of thrombin there still remained a part of fibrinogen binding inhibition although aggregation was not impaired. Electrophoretic and immunoelectrophoretic studies showed no difference before and after treatment by PCR 4099. In particular, the GP IIb-IIIa-complex

was not dissocd., its electrophoretic mobility was not changed and three monoclonal anticomplex antibodies recognized it in the same manner before and after treatment. Apparently, PCR 4099 selectively inhibits the ADP aggregation pathway and that the inhibition of fibrinogen binding is probably not due to a direct modification of the GP IIb-IIIa complex.

L7 ANSWER 9 OF 21 COPYRIGHT 1992 ACS
TI Crystal and molecular structure of methyl .alpha.-6,7-dihydrothieno[3,2-c]pyrid-5(4aH)-yl(o-chlorophenyl)acetate camphosulfonate. Absolute configuration
SO Z. Kristallogr., 188(1-2), 85-93
AU Enjalbert, R.; Galy, J.; Gehenot, A.; Rao, R.; Maire, G.; Frehel, D.
PY 1989
AN CA112(6):46093s
AB The abs. configuration of the title compd. which shows a pharmacol. activity was detd. by the Bijvoet difference method. The compd. is orthorhomibic, space group P212121, with a = 10.292(2), b 12.777(2), c 20.471(2) .ANG.; Z = 4. The final values are R = 0.031 and Rw = 0.032 for 2920 reflections. At. coordinates, bond lengths and angles are given. The camphosulfonate modulus A, has an R configuration and the Me .alpha.-(6,7-dihydrothieno(3,2-c)pyrid-5(4aH)-yl)(o-clorophenyl)acetate, modulus B, exhibits an S configuration.

L7 ANSWER 10 OF 21 COPYRIGHT 1992 ACS
TI Preparation of d-.alpha.-5-(4,5,6,7-tetrahydro[3,2-c]thienopyridyl)-2-(chlorophenyl) acetic acid methyl ester as an antithrombotic
SO Jpn. Kokai Tokkyo Koho, 10 pp.
PI JP 63203684 A2 23 Aug 1988 Showa
AI JP 88-34943 16 Feb 1988
PY 1988
AN CA110(21):192801w
GI

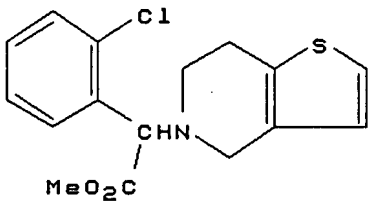


I

AB The title compd. d-(I) inhibiting blood platelet aggregation was prepd. by resoln. of dl-I with an optically active acid. dl-I (0.0994 mol) was dissolved in 150 mL Me2CO and 0.0397 mol l-camphor-10-sulfonic acid (II), H2O was added. The resulting clear soln. was left to stand at room temp. After 48 h some crystals were formed. The mixt. was concd. to 50 mL and was kept at room temp. for 24 h to give 55% (based on dl-I) I.II salt which was recrystd. from 50 mL Me2CO to give 88% salt. The latter in H2O was cooled to 5.degree. and made alk. with satd. NaHCO3 and extd. with CH2Cl2 to give quant. d-I. Platelet rich plasma prepd. from blood samples of rats who were administered with dl-I 4.48, d-I 5, and l-I 40 mg/kg orally 2 h prior to blood sampling inhibited ADP-induced blood platelet aggregation by 30, 67, and 13% resp.

L7 ANSWER 11 OF 21 COPYRIGHT 1992 ACS

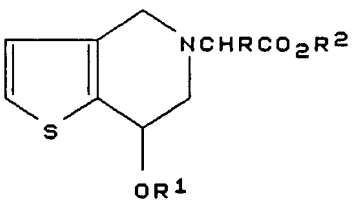
TI Effect of PCR 4099 on ADP-induced calcium movements and phosphatidic acid production in rat platelets
SO Biochem. Pharmacol., 37(13), 2559-64
AU Feliste, Rosette; Simon, Marie Francoise; Chap, Hugues; Douste-Blazy, Louis; Defreyn, Ghislain; Maffrand, Jean Pierre
PY 1988
AN CA109(13):104428f
GI



I

AB Antiplatelet activity of PCR 4099 (I), an analog of ticlopidine, resides in its specific effect against exogenous as well as released ADP. The effects of the drug on ADP-induced shape change, elevation of cytosolic free Ca2+ concn. ([Ca2+]i) and hydrolysis of inositol phospholipids, monitored as [32P]phosphatidic acid formation, were studied in rat platelets. Shape change and influx of Ca2+ across the plasma membrane were not modified after PCR 4099 addn. to aspirin-treated platelets. On the other hand, phosphatidic acid formation and Ca2+ mobilization from internal stores were strongly inhibited. These results suggest that PCR 4099 leaves intact the machinery involved in ADP-induced platelet shape change and influx of Ca2+ but inhibits an early step in the ADP-response coupling leading to inositol phospholipid hydrolysis and aggregation.

L7 ANSWER 12 OF 21 COPYRIGHT 1992 ACS
TI Preparation of 6,7-dihydro-.alpha.-phenyl-thieno[3,2-c]pyridine-5(4H)-acetates as antithrombotics
SO Fr. Demande, 17 pp.
AU Frehel, Daniel; Maffrand, Jean Pierre; Vallee, Eric; Badorc, Alain
PI FR 2597102 A1 16 Oct 1987
AI FR 86-5818 14 Apr 1986
PY 1987
AN CA109(9):73415t
GI



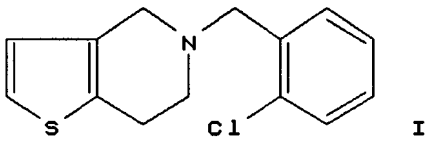
I

AB The title compds. [I; R = (un)substituted Ph; R1 = R2, R3CO; R2 = H, (un)satd. alkyl, (un)substituted aralkyl; R3 = alkyl, (un)substituted aryl, aralkyl], their stereoisomers and pharmaceutically acceptable salts, were prepd. as blood platelet aggregation inhibitors, useful as antithrombotics.

4,5,6,7-Tetrahydrothieno[3,2-c]pyridin-7-ol-HCl and 2-ClC6H4CHClCO2Me were heated 3 h at 70.degree. in DMF contg. K2CO3 to give I (R = 2-ClC6H4, R1 = H, R2 = Me) (II), as a mixt. of 2 diastereomers. Blood plasma from rats receiving 200 mg II/kg/day orally for 3 days had a 51% redn. in collagen-induced platelet aggregation, compared to 32% for ticlopidine.

L7 ANSWER 13 OF 21 COPYRIGHT 1992 ACS
TI Broad spectrum anti-platelet activity of ticlopidine and PCR 4099 involves the suppression of the effects of released ADP
SO Thromb. Res., 48(4), 403-15
AU Feliste, R.; Delebassee, D.; Simon, M. F.; Chap, H.; Defreyn, G.; Vallee, E.; Douste-Blazy, L.; Maffrand, J. P.
PY 1987
AN CA108(11):87784d
GI

(b)

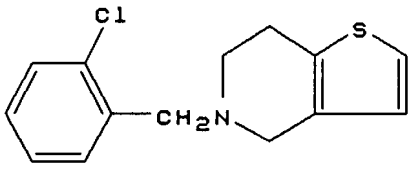


AB Aggregation and serotonin secretion were studied in washed rat platelets after oral administration of ticlopidine (I) or its more potent analog PCR 4099. Besides a complete suppression of the ADP-induced aggregation, the 2 drugs inhibited aggregation and secretion induced by 3 protein kinase C activators, (1-oleoyl-2-acetyl-sn-glycerol, 12-O-tetradecanoyl phorbol-13-acetate, and phospholipase C, by the Ca2+ ionophore A 23187, and by thrombin. The highest inhibition was obsd. at low stimuli concns. but could be partly or almost completely overcome by increasing their concns. The combination of aspirin (ASA) with the ADP scavenging system, creatine phosphate/creatine phosphokinase (CP/CPK) in vitro resulted in an inhibition similar to that obsd. ex vivo after ticlopidine or PCR 4099 treatment. Moreover, these in vitro and ex vivo treatments were not additive. As identical results were obtained with CP/CPK alone but not with ASA, it is concluded that ticlopidine and PCR 4099 do not interfere with protein kinase C or Ca2+ movements but specifically inhibit the effects of released ADP, which might explain the broad spectrum anti-platelet activity of these drugs.

L7 ANSWER 14 OF 21 COPYRIGHT 1992 ACS
TI Inhibition of the thrombocytopenic effect of exogenous and endogenous thrombin by PCR 4099 ((d,1)methyl-2-(2-chlorophenyl)-2(4,5,6,7-tetrahydrothieno-(3,2-c)pyridin-5-yl)acetate.cntdot.hydrochloride.cntdot.monohydrate)
SO Thromb. Res., 48(5), 585-9
AU Damas, J.; Grek, V.; Remacle-Volon, G.
PY 1987
AN CA108(9):68616j
AB In rats, orally administered PCR 4099 (I) inhibited the thrombocytopenic effects of i.v. thrombin and ellagic acid; however, the thrombocytopenic effect of i.v. .lambda.-carrageenan was not inhibited by I. I failed to prevent the hypotensive effect of arachidonic acid in rats suggesting that I does not inhibit cyclooxygenase. Possible mechanisms of the actions of I are

discussed.

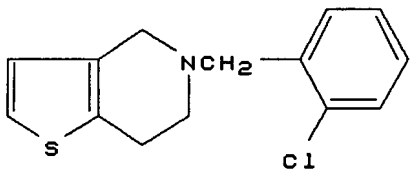
L7 ANSWER 15 OF 21 COPYRIGHT 1992 ACS
TI Mechanism of interaction of ticlopidine and its analogs with the energy-conserving mechanism in mitochondria
SO Biochem. Pharmacol., 35(11), 1855-9
AU Abou-Khalil, Samir; Abou-Khalil, Wafa H.; Yunis, Adel A.
PY 1986
AN CA105(5):35376r
GI



I

AB The mechanism of interaction of ticlopidine (I) [55142-85-3] and its analogs with the energy-conserving mechanisms in mitochondria was studied in isolated rat liver. The transport of phosphate [14265-44-2], glutamate [56-86-0] and succinate [110-15-6] into mitochondria was not affected significantly by ticlopidine or any of its analogs; however, it was inhibited by both mersalyl and N-ethylmaleimide. There was no inhibitory effect on the tested drugs on the mitochondrial 3H-labeled ADP [58-64-0] translocation activity; rather, ticlopidine produced a concn.-dependent increase of that activity, reaching 54% with 20 .mu.g/mL. Ticlopidine and its analog, PCR 5325 [55157-56-7] increased the latent ATPase [9000-83-3] activity by about 400% and the DNP-dependent ATPase by about 50%. Also, PCR 4099 [90055-48-4] caused a 115% increase in the latent activity, whereas the effects of the remaining analogs varied from slight activation to slight inhibition. Under nonphosphorylation conditions, the mitochondrial H+ extrusion resulting from succinate oxidn. was inhibited by ticlopidine in a concn.-dependent manner, reaching a quasi total inhibition with 40 .mu.g/mL. While PCR 5325 gave results similar to ticlopidine, PCR 4099 was less inhibitory and the other analogs were ineffective. These data indicate that the inhibitory action caused by ticlopidine and some of its analogs on oxidative phosphorylation does not reside at one particular site in the mitochondrial membrane; rather, the inhibition seems to be the outcome of profound alterations in mitochondrial ADP translocase, latent ATPase, and proton translocation in the respiratory chain.

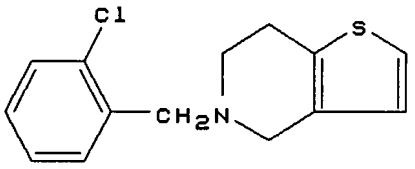
L7 ANSWER 16 OF 21 COPYRIGHT 1992 ACS
TI Effects of ticlopidine, a new platelet antiaggregating agent, and its analogs on mitochondrial metabolism. Oxidative phosphorylation, protein synthesis and DNA polymerase activity
SO Biochem. Pharmacol., 33(23), 3893-8
AU Abou-Khalil, Wafa H.; Lim, Lori O.; Yunis, Adel A.; Abou-Khalil, Samir
PY 1984
AN CA102(9):72600t
GI



I

AB The effects of ticlopidine (I) [55142-85-3] and 6 of its analogs on mitochondrial functions were studied in isolated rat liver mitochondria. The influence of ticlopidine and each of the following analogs: PCR 5325 [94188-86-0], PCR 4099 [94188-84-8], PCR 3787 [94188-83-7], PCR 2362 [82350-97-8], PCR 4499 [94188-85-9], and PCR 0665 [94188-82-6] was evaluated by detg. their interaction with 3 major mitochondrial activities. Oxidative phosphorylation, measured by oxypolarog., was assayed in the presence of glutamate or succinate as source of energy, and both State 4 and State 3 were recorded. Ticlopidine, at 20 .mu.g/mL, slightly increased glutamate State 4, whereas it was without effect on that of succinate. At higher concn. (40 .mu.g/mL), ticlopidine caused 40-45% inhibition of State 4 with both substrates. All the other analogs tested at either 20 or 40 .mu.g/mL were virtually without effect on the respiration. However, at 20 .mu.g/mL, ticlopidine and some of its analogs inhibited mitochondrial State 3, while under similar conditions other analogs had little or no effect on this state. Mitochondrial protein synthesis, measured by [14C]-L-leucine incorporation, was not affected significantly by any of these drugs. Whereas chloramphenicol at 10 .mu.g/mL caused 80% inhibition, ticlopidine and its analogs in concns. inhibitory to State 3 did not inhibit mitochondrial protein synthesis. Mitochondrial DNA polymerase [9012-90-2] activity, detd. by [3H]thymidine 5′-triphosphate incorporation, was not inhibited by these drugs. Thus, while ticlopidine and analogs have little or no effect on either mitochondrial protein synthesis or mitochondrial DNA polymerase activity, ticlopidine and some of its analogs are inhibitory of the energy conserving mechanism in mitochondria.

L7 ANSWER 17 OF 21 COPYRIGHT 1992 ACS
TI Comparative effects of ticlopidine and analogs on in vitro myeloid colony (CFU-GM) growth
SO Agents Actions Suppl., 15(Ticlopidine: Quo Vadis?), 136-47
AU Yunis, Adel A.; Arimura, Grace K.; Lo, Lilian
PY 1984
AN CA102(5):39648s
GI

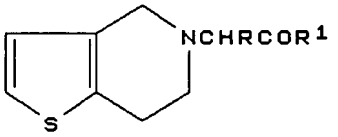


I

AB Ticlopidine (I) [55142-85-3] and its 6 analogs inhibited granulocyte-macrophage progenitor cell (CFU-GM) growth in both mouse and human bone marrow at concns. of .gtoreq.10 .mu.g/mL. Their

inhibitory effect in the order from the most to the least inhibitory was PCR 3787 [94188-83-7] .gtoreq. PCR 4499 [94188-85-9] > I = PCR 5325 [94188-86-0] > PCR 4099 [94188-84-8] > PCR 2362 [82350-97-8] > PCR 0665 [94188-82-6]. Growth inhibition by I analogs was not specific for CFU-GM. The growth of erythroid as well as lymphoid cells was also inhibited. Thus, these studies suggest that the hematol. complications of I may be related to a direct toxication of the drug on bone marrow cells.

L7 ANSWER 18 OF 21 COPYRIGHT 1992 ACS
TI Thieno[3,2-c]pyridine derivatives and their therapeutical use
SO Eur. Pat. Appl., 20 pp.
AU Aubert, Daniel; Ferrand, Claude; Maffrand, Jean Pierre
PI EP 99802 A1 1 Feb 1984
AI EP 83-401382 5 Jul 1983
PY 1984
AN CA100(23):191856z
GI



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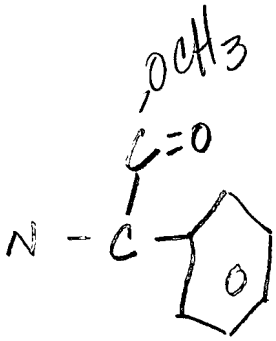
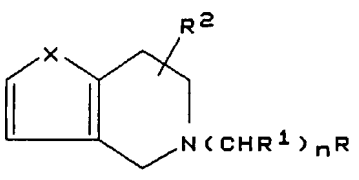


AB Thienopyridines I (R = Ph, substituted Ph; R1 = OH, alkoxy, amino), useful as platelet aggregation inhibitors, were prepd. Thus, I (R = 2-ClC6H4, R1 = OMe) was obtained in 45% yield by treating 4,5,6,7-tetrahydrothieno[3,2-c]pyridine with 2-ClC6H4CHClCO2Me. At 3 .times. 5 mg/kg orally in rats I (R = 2-ClC6H4, R1 = OMe) increased the bleeding time from 420 to 1080 s.

L7 ANSWER 19 OF 21 COPYRIGHT 1992 ACS
TI Therapeutic compositions having antithrombotic and anti-blood-platelet-aggregating activity
SO Can., 27 pp.
AU Blanchard, Jean; Panak, Edouard
PI CA 1147658 A1 7 Jun 1983
AI CA 80-342967 3 Jan 1980
PY 1983
AN CA99(18):146116h
GI



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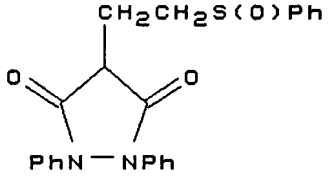
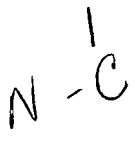


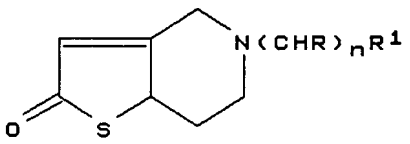
II



AB A combination of furo- or thienopyridines (I, X = O or S, R = Ph, PhCO or substituted benzoyl; R1 = H, halo, OH, lower alkyl, alkoxy, or Ph; R2 = lower alkyl and n = 1-15) and sulfinpyrazone (II) [57-96-5] has antithrombotic and blood platelet aggregation inhibition activities and may be used in oral dosage forms. Thus,

tablets were prepd. contg. 0.150 g ticlopidine-HCl (I, X = S, R1 = R2 = H, R = 2-ClC6H4, n = 1;.HCl) [53885-35-1], and 0.075 g II. Poly(vinylpyrrolidone), corn starch and Mg stearate and talc were used as excipients.

L7 ANSWER 20 OF 21 COPYRIGHT 1992 ACS
TI Thienopyridinone derivatives and their therapeutic use
SO Fr. Demande, 23 pp.
AU Boigegrain, Robert; Maffrand, Jean Pierre; Suzuki, Norio; Matsubayashi, Kiuichi; Ashida, Shinichiro
PI FR 2495156 A1 4 Jun 1982
AI FR 80-25274 28 Nov 1980
PY 1982
AN CA97(23):198186j
GI



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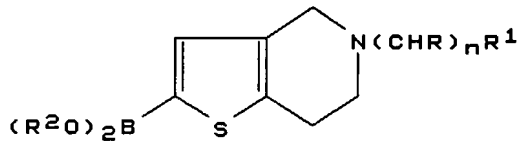
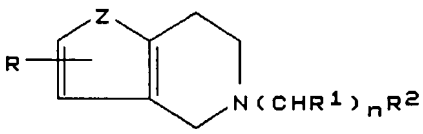


II

AB Tetrahydrothienopyridinones I (n = 0, 1, 2, 3, 4; R = H, alkyl; R1 = H, Ph, halo-, alkoxy-, alkyl-, nitro-, carboxy-, carbalkoxy-, or cyanophenyl), which inhibited blood platelet aggregation, were prepd. from the resp. boronic acids II (R2 = H, alkyl). II (n = 1, R = H, R1 = 2-NCC6H4, R2 = H) in THF was treated with H2O2 to give I (n = 1, R = H, R1 = 2-NCC6H4).

L7 ANSWER 21 OF 21 COPYRIGHT 1992 ACS
TI Thienopyridine derivatives
SO Rom., 7 pp.
AU Castaigne, Albert Rene Joseph
PI RO 63529 6 Jul 1978
AI RO 74-77913 5 Mar 1974
PY 1978
AN CA92(5):41917x
GI



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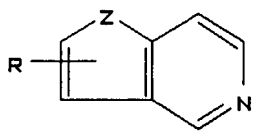

II

AB Thieno- and furopyridines I (Z = O, S; R = H, halo; n = 1-3; R1 = H, OH, alkyl; R2 = Ph, halo-, alkyl-, alkoxy-, hydroxy-, or nitrophenyl, PhCH2, halo-, alkyl-, alkoxy-, hydroxy-, or nitrobenzyl), which showed antiinflammatory and vasodilator activity and inhibited blood platelet aggregation, were prepd. by quaternizing II with R2(CHR1)nX (X = halo) followed by hydride redn. Thus, treating II (Z = S, R = H) with 2-ClC6H4CH2Cl gave a

quaternary salt which was treated with NaBH4 12 h to give I (Z = S, R = R1 = H, n = 1, R2 = 2-ClC6H4).

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